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No. 343

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IN THE

Supreme Court of the United States

OCTOBER TERM, 1968

UNITED STATES OF AMERICA,
Petitioner,

v.

AN ARTICLE OF DRUG * * * BACTO-UNIDISK * * *

On Writ of Certiorari to the United States Court of Appeals for the Sixth Circuit

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BRIEF FOR CLAIMANT DIFCO LABORATORIES, INC.

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BRIEF FOR CLAIMANT DIFCO LABORATORIES, INC.

QUESTION PRESENTED

Whether a sensitivity disk utilized as part of a laboratory testing procedure which yields information the physician may use as a guideline to the changing or selection of an antibiotic to treat patients who have not responded to initial therapy, is a "drug" within the meaning of Section 201(g)(1)(B) of the Federal Food, Drug, and Cosmetic Act and, if it is a "drug", whether it is subject to batch certification under Section 507 of the Act.

STATUTE INVOLVED.

The Federal Food, Drug, and Cosmetic Act, 52 Stat. 1040 (1938), as amended, 21 USC 301 et seq., provides in part:

Sec. 201 (21 USC 321)

(j) The term "official compendium" means the official United States Pharmacopeia . . . official National Formulary, or any supplement to any of them.

* * * *

(n) If an article is alleged to be misbranded because the labeling is misleading, then in determining whether the labeling is misleading there shall be taken into account (among other things) not only representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article to which the labeling relates under the conditions of use prescribed in the labeling thereof or under such conditions of use as are customary or usual.

Sec. 301 (21 USC 331)

The following acts and the causing thereof are hereby prohibited:

(a) the introduction or delivery for introduction into interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded.

* * * *

(d) the introduction or delivery for introduction into interstate commerce of any article in violation of section . . . 505.

* * * *

(f) The refusal to permit entry or inspection as authorized by section 704.

* * * *

(p) The failure to register as required by section 510.

* * * *

Sec. 303 (21 USC 333)

(a) Any person who violates any of the provisions of section 301 shall be guilty of a misdemeanor and shall on conviction thereof be subject to imprisonment for not more than one year, or a fine of not more than $1,000, or both such imprisonment and fine; but if the violation is committed after a conviction of such person under this section has become final such person shall be subject to imprisonment for not more than three years, or a fine of not more than $10,000, or both such imprisonment and fine * * *

(b) Not withstanding the provisions of subsection (a) of this section, in case of a violation of any of the provisions of section 301, with intent to defraud or mislead, the penalty shall (except in the case of an offense which is subject to the provisions of the proviso to subsection (a) relating to second or subsequent offenses) be imprisonment for not more than three years, or a fine of not more than $10,000, or both such imprisonment and fine.

* * * *

Sec. 403 (21 USC 343)

A food shall be deemed to be misbranded . . . (c) If it is an imitation of another food, unless its label bears . . . the word "imitation" and, immediately thereafter, the name of the food imitated.

* * * *

(g) If it purports to be or is represented as a food for which a definition and standard of identity has been prescribed by regulations as provided by section 401, unless

(1) it conforms to such definition and standard, and (2) its label bears the name of the food specified in the definition and standard, and, insofar as may be required by such regulations, the common names of optional ingredients (other than spices, flavoring, and coloring) present in such food.

* * * *

Sec. 501 (21 USC 351)

A drug or device shall be deemed to be adulterated-(a) . . . (2) . . . (B) if it is a drug and the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this Act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess; or (3) if it is a drug and its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health; or (4) if (A) it is a drug which bears or contains, for purposes of coloring only, a color additive which is unsafe within the meaning of section 706(a), or (B) it is a color additive the intended use of which in or on drugs is for purposes of coloring only and is unsafe within the meaning of section 706(a).

(b) If it purports to be or is represented as a drug the name of which is recognized in an official compendium, and its strength differs from, or its quality or purity falls below, the standard set forth in such compendium . . .

(c) If it is not subject to the provisions of paragraph (b) of this section and its strength differs from, or its purity or quality falls below, that which it purports or is represented to possess.

Sec. 502 (21 USC 352)

A drug or device shall be deemed to be misbranded—

(a) If its labeling is false or misleading in any particular.

* * * * *

(f) Unless its labeling bears (1) adequate directions for use; and (2) such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users: *Provided*, That where any requirement of clause (1) of this paragraph, as applied to any drug or device, is not necessary for the protection of the public health, the Secretary shall promulgate regulations exempting such drug or device from such requirement.

(g) If it purports to be a drug the name of which is recognized in an official compendium, unless it is packaged and labeled as prescribed therein: *Provided*, That the method of packing may be modified with the consent of the Secretary.

* * * * *

(j) If it is dangerous to health when used in the dosage, or with the frequency or duration prescribed, recommended, or suggested in the labeling thereof.

* * * *

Sec. 505 (21 USC 355)

(a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) is effective with respect to such drug.

(b) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Sec-

retary as a part of the application (1) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (2) a full list of the articles used as components of such drug; (3) a full statement of the composition of such drug; (4) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (5) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (6) specimens of the labeling proposed to be used for such drug * * *

Sec. 507 (21 USC 357)

'(f) Any interested person may file with the Secretary a petition proposing the issuance, amendment, or repeal of any regulation contemplated by this section. The petition shall set forth the proposal in general terms and shall state reasonable grounds therefor. The Secretary shall give public notice of the proposal and an opportunity for all interested persons to present their views thereon, orally or in writing, and as soon as practicable thereafter shall make public his action upon such proposal. At any time prior to the thirtieth day after such action is made public any interested person may file objections to such action, specifying with particularity the changes desired, stating reasonable grounds therefor, and requesting a public hearing upon such objections. The Secretary shall thereupon, after due notice, hold such public hearing. As soon as practicable after completion of the hearing, the Secretary shall by order make public his action on such objections. The Secretary shall base his order only on substantial evidence of record at the hearing and shall set forth as part of the order detailed findings of fact on which the order is based. The order shall be subject to the provisions of section 701(f) and (g).

* * * *

Sec. 701 (21 USC 371)

* * * (f) (1) In a case of actual controversy as to the validity of any order under subsection (e), any person who will be adversely affected by such order if placed in effect may at any time prior to the ninetieth day after such order is issued file a petition with the Circuit Court of Appeals of the United States for the circuit wherein such person resides or has his principal place of business, for a judicial review of such order. A copy of the petition shall be forthwith transmitted by the clerk of the court to the Secretary or other officer designated by him for that purpose. The Secretary thereupon shall file in the court the record of the proceedings on which the Secretary based his order, as provided in section 2112 of title 28, United States Code.

* * * *

(f) (6) The remedies provided for in this subsection shall be in addition to and not in substitution for any other remedies provided by law.

* * * *

SUMMARY OF ARGUMENT

The antibiotic disk sensitivity test is used to obtain an indication of whether an infectious organism which has proved resistent to an antibiotic drug or drugs administered *before* the results of the test have been obtained, is sensitive *in vitro* to another drug or drugs. If the organism is sensitive *in vitro* to a particular antibiotic, that drug may be suitable for treatment of the patient suffering from the infection. Whether, if found sensitive *in vitro*, it would be administered to the patient, would depend upon many factors taken into consideration by the physician, other than the results of the test.

The physician always has a choice of more than one antibiotic both before and after the test is run. There

are many built-in protections which preclude the choice of the wrong antibiotic as the result of the use of a faulty disk in a sensitivity test. These are reviewed in Point I of the Argument and apparently were ignored or not understood at the time the Food and Drug Administration decided that disks should be made subject to certification. That proceeding did not involve the particular disk before the court and, in any event, no review of the decision by the Court of Appeals was available to any party (Point V).

The testimony and findings show that the disk is not used in "diagnosis" or "treatment" and is not a "drug" for that reason alone. Further, it is not a "drug" because it is not used in or on the body. The principal argument of the Government—that the disk should be classified as a drug to protect the public—would involve an unconstitutionally vague application of the statute (Point II).

The certification provisions of Section 507 of the statute would not be applicable to the disk, even if it were used in "diagnosis" or "treatment" of disease within the meaning of Section 201(g)(1)(B), and were therefore a "drug" under that section, because only antibiotic drugs administered or applied to patients were intended by Congress to be subject to certification.

ARGUMENT

Introduction

1. The statement of the Question Presented (Pet. Br. 2) is inaccurate and misleading.

Thus, to pose the question of whether sensitivity disks "containing various antibiotic drugs" are "antibiotic drugs" under the Act prejudges the very point at issue. The obvious and necessary implication is that the chemicals on the disks are drugs in some sense, presumably in

the common understanding of that term, i.e., that they are medicines (Webster's New International Dictionary). The implication is misleading. The chemicals are not available for use as drugs, not being in dosage form and being suitable only for use in laboratory testing procedures.

Moreover, the fact that Bacto-Unidisks contain chemicals commonly used as drugs, i.e., antibiotic substances and sulfadiazine, has nothing to do with the question of whether the disk itself is a drug since, as the court of appeals recognized, it is the "intended use" of an article which determines whether it falls within the definition of "drug", i.e., whether it is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease (App. 201).[1] Thus, neither the disk itself nor the chemicals with which it is impregnated are drugs unless intended for such use.

The phrase in the Question Presented, "disks which physicians use to select the antibiotic most appropriate to treat a particular patient", being unqualified, conveys the idea that before an antibiotic is administered by the physician the disk indicates the proper drug to be used for the particular condition of the patient. This is not in accordance with the evidence. It is shown in the Argument that it is not the disk but the information derived from the entire testing procedure which may be used by the physician when he receives it—ordinarily some 24 to 36 hours or more after initial therapy has begun. Moreover, it is the laboratory worker who "uses" the disk and reports to the clinician.

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[1] As the court of appeals also noted (App. 201), even honey may be a "drug" under the Act if it is intended for use in the treatment of disease within the meaning of Sec. 201(g)(1)(B); but surely no rational person would suggest that its use in a laboratory testing procedure would constitute a use in the treatment of disease.

The Question Presented in the petition has been restated for the reasons set forth above.

2. The Government's statement of the case presages some of the dubious and unsupportable positions advanced in its argument.

It is the Government's contention that the public health need which Congress saw in 1947 for the certification of penicillin (and later for other antibiotic drugs) is translatable to a need for the certification of sensitivity disks used for laboratory testing, because they bear antibiotic substances and because certification is allegedly needed to assure the safety and efficacy of use of antibiotics administered to patients.[2] The argument will not stand examination. It is fully clear that the legislative record discussed in the brief was based on the need for certification of antibiotic drugs administered to or applied to patients. The record is entirely inconsistent with any other interpretation, as is demonstrated in Point III, *infra*. Sensitivity disks are not administered to or applied to patients in any way and the disks were not even in existence commercially when the certification provisions of the statute (Section 507) were enacted in 1945 (App. 126). The history recited in the brief is therefore irrelevant to the question of certification of the disks and lends no support to the Government's attempt to find a public health issue which it hopes will sway this court.

As we shall show, the effort to equate the need seen by Congress for the certification of dosage forms of antibiotic drugs with the alleged need for certification of sensitivity disks is not supported by any probative evidence adduced at the trial of this case in the District

[2] The notion that the disks should be controlled on the ground that control is necessary to assure safety and efficacy of use of other products, i.e., antibiotics administered to patients, is not relevant to Section 507. If disks are certifiable it is because of the nature and use of the disks, not because of the nature and use of other products.

Court. Nor is it supported by the extra-record publications cited, for the first time, in the Government's brief in this Court.[3]

I.

There is no Public Health Reason for the Certification of Antibiotic Sensitivity Disks

A. *Basic Considerations*

The brief for the United States pictures the Bacto-Unidisk (and other sensitivity disks) as dreadfully dangerous articles which need close government supervision in order to save the lives of patients. The difficulty is that (a) the principal basis for the attempted shock treatment is a series of publications *dehors* the record in the trial court with respect to which neither the authors nor any expert witness were subject to examination by claimant Difco Laboratories, Inc.[4] and (b) the ultimate conclusions drawn in the Government's brief from the publications in question are erroneous and unsound and show a basic lack of understanding of the function of sensitivity disks.

It is improper and grossly unfair to the claimant for the Government to go through a trial on the merits of the question of whether the Bacto-Unidisk is a drug without even attempting to support its case with the publications in question or with testimony of their authors, and then, for the first time in this court to ask the court to con-

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[3] *E.g.*, Greenberg and Fitzpatrick, *On the Control of Antibiotic Disks in Canada*, 79 Canadian Medical Association Journal 383 (1958) (Pet. Br. 22), state that faulty disks "present a serious health hazard", but offer no facts to support the assertion.

[4] With the exception of Dr. Truant (Ph. D.). He was the only author presented as a witness at the trial. His testimony is discussed, *infra*.

sider them in arriving at its decision.[5] It is one thing for the court to take judicial notice of commonly-known facts. It is quite a different matter for the court to take such notice of opinions such as those of officials of the Canadian Department of Health and Welfare which are not even supported by facts.[6]

It will be shown that the alarming and foreboding assertions of the Government of the dangers of faulty disks are not substantiated factually either by the literature cited or by the testimony at the trial in the District Court. They were originally put forward in the rule-making proceedings of 1960 and 1961 (Pet. Br. 8-9) on the basis of certain complaints referred to in the Government's brief, but without adequate consideration of the following factors.

(1) The physician always has a choice of more than one antibiotic—a "battery" of them, as Dr. Keefer put it (App. 73-74, 120). It is not accurate to imply that the physician relies principally on the disk to select the antibiotic that is "best for administration to his patient" (Pet. Br. 23-24). In addition to the "battery" from which he may choose, the physician has many sources of information to guide him in that choice (App. 76-77), and the location or type of infection, the condition of the patient, the toxicology and pharmacology of the antibiotic, are among the factors upon which he must base the choice. See the discussion in Goodman and Gilman, *The Pharmacological Basis of Therapeutics*, 3rd Ed. 1965, Chap. 56,

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[5] It has long been settled that this court may not properly refer to evidentiary matters not contained in the record certified to the court by the Court of Appeals. *New York Indians* v. *United States*, 170 U.S. 1; *McClellan* v. *Carland*, 217 U.S. 268; *Lawn* v. *United States*, 355 U.S. 339. We know of no exception to this rule applicable to hearsay scientific documents. Compare *New York Indians* v. *United States*, *supra*, where this court held it proper to take judicial notice of statutes or official public documents.

[6] See Note 3, *supra*.

1171 et seq. (Pet. Br. 15). Moreover, as the testimony at the trial and the publications cited by the Government clearly reveal, it is not the physician (clinician) but a laboratory worker who uses the disks.

(2) As all witnesses agreed, it is common practice for the physician to prescribe one or more of this "battery" of antibiotics, on the basis of his experience and the information available to him from various sources, *before* a sensitivity test is run (App. 61, 73, 121, 143-144, Finding Number 8, App. 194). This is "almost always" done according to a Government witness (App. 143-144).

Known antibiotics are classified as to their respective areas of basteriostatic or bactericidal activity and the facts of such classification are well known to physicians. For example, Dr. Weinstein, who wrote Chapter 56 of Goodman & Gilman, *supra*, lists the drug order of choice of 37 antimicrobial agents for use against more than 60 infectious organisms which cause many serious diseases (pp. 1176-1180). Obviously, with this and similar information available, physicians are ordinarily in a position to prescribe antibiotics and, in the vast majority of cases, the prescription will not have to be changed on the basis of a sensitivity test, assuming such a test is run.

The Government notes that the labeling of Bacto-Unidisks states that they are "especially valuable in selecting the drug effective against chronic or persistent infections refractory to primary therapy" (Pet. Br. 11). By "primary therapy" is meant therapy begun *before* a sensitivity test is run, the usual practice.

The statement on page 18 of the Government's brief that batch-testing ". . . is a method of assuring that, when the physician prescribes a particular antibiotic, the patient gets the treatment which the physician intended" is misleading when related to disk-sensitivity testing procedures since (a) initial or primary therapy is almost al-

ways underway when the test results are received from the laboratory and (b) such results are but one of the many sources of information relied upon by the physician. It is quite obvious from the record and the literature cited by the Government that the emphasis in the Government's argument upon the results of the disk test is wholly misplaced. No careful physician would rely so heavily upon such tests which, as Dr. Keefer testified, are the least sensitive quantitatively of the several sensitivity tests available (App. 113).

(3) Dr. Keefer testified that he knew of no public health problem resulting from faulty sensitivity disks and that he had had no experience with the administration of the wrong antibiotic caused by an inaccurate test "because in such instances where such a question may arise, the patient is usually getting one, two, three, and sometimes four different antibiotics if he is desperately ill" (App. 126).

Dr. Truant and Dr. Lerner thought that faulty disks would create a public health problem but both admitted on cross-examination that they could not cite any instance of harm to a patient resulting from the use of a faulty disk in a sensitivity test (App. 93-94, 141). Nor did they even point to a particular instance where faulty disks had affected the validity of the information given to the physician.

Dr. Truant said "I cannot put my finger on it now, but recall that there were a number of instances brought to my attention by individuals in the infectious disease department" (App. 93). If Dr. Truant had been told by "individuals in the infectious disease department" (presumably meaning medical doctors) that his laboratory had given a physician information which misled the physician to a patient's detriment, it is difficult to believe that Dr. Truant would not have remembered the circumstances.[7]

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[7] Dr. Truant did not testify on the alleged health problem until he had completed direct and cross-examination and was recalled.

Petersdorf and Sherris [8] (Pet. Br. 5-6, Note 2) state:

> "Finally it must be emphasized that the course of clinical infections is subject to many more variables than the chemotherapeutic. In our experience, failure of antimicrobial therapy is far more often related to one of these variables than to choice of the incorrect drug. It is not the purpose of this discussion to dwell in detail on the causes for failure of chemotherapy. However, 'choice of the incorrect drug' has been blamed for therapeutic failures all too often, when in actuality failure to relieve a focus of obstruction, to drain an abscess, to ignore evidence of a superinfection or a hypersensitivity reaction, or to attempt treatment of nonbacterial infections, *are the reasons responsible* for unsuccessful chemotherapy. (pp. 775-776, emphasis supplied).

This statement is totally at variance with the frightening prospect of patient injuries resulting from selection of the wrong drug if sensitivity disks are not subject to certification, which has been conjured up by the Government.

The article by Greenberg and Fitzpatrick,[9] cited in support of the argument that uncertified disks are a health hazard shows only that the regulatory agency in Canada agrees with the regulatory agency in the United States. In all of the extra-record citations made in the Government's brief, only in the article by officials of the Canadian regulatory agency have we found the opinion expressed that the result of a test with a faulty disk might be a serious hazard to a patient.

For the reasons herein stated we think it clear that both agencies are wrong, entirely aside from the question of law involved under the Federal Food, Drug, and Cosmetic

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[8] *Methods and Significance of In Vitro Testing of Bacterial Sensitivity to Drugs* 39 American Journal of Medicine 766 (1965).

[9] *Supra*, Note 3 at 383.

Act. Neither the Canadian regulatory officials nor those of the Food and Drug Administration, either in a publication or at the trial in the lower court, have produced a single instance of harm to a patient resulting from the use by the physician of information derived from a disk test or any other factual evidence that hazards are involved in the use of faulty disks. The reason is that it is practically inconceivable that such a thing could happen, with all the built-in protections which we describe herein. Doubtless if we had been given the opportunity to cross-examine the authors of the Canadian publication they, like Dr. Truant and Dr. Wolfe at the trial, would have been unable to document their general statements that a health hazard is involved.

It is of interest to note that in Greenberg, Fitzpatrick, and Branch, *The Status of the Antibiotic Disc in Canada*, 76 Canadian Medical Association Journal 194 at 196 (1957) it is stated that ". . . unless grossly faulty disks are being used, they may still give useful results and may serve to differentiate between highly sensitive and very resistant strains. A careful study of the results in the table will show that because of this feature the majority of discs assayed would probably yield satisfactory tests in spite of their off potencies".

It cannot be doubted that, had the Government found any hard evidence of danger from faulty disks it would have produced it during the six years of this litigation.

It is true that the size of the zone of inhibition can be influenced by the amount of antibiotic on the disk. It can also be influenced equally by other factors, including—

(1) Density of inoculum
(2) Purity of inoculum
(3) pH of medium
(4) Depth of medium

(5) Composition of medium
(6) Temperature and time of incubation
(7) Cleanliness of glassware
(8) Contact of the chemical on the disk with the medium.[10]

All of these factors must be taken into consideration by the technician just as he must consider the variations in the amount of antibiotic substance on the disk.

It does not follow from this, as the Government would have it, that the technician is going to be fooled by variations in zone size (See I-B, *infra*). It does follow, however, that the statements about the public health being threatened by one of the factors involved—the amount of chemical on the disk—have little if any probative value in the absence of documented mistakes related to that factor. Such documentation has never been presented. As Dr. Lerner, a Government witness, said at the trial, ". . . there have been results of tests . . . which I have discarded because they were not coincident with the rest of the information concerning the condition of the patient in question" (App. 141) but, obviously, this is what any careful clinician would do.

(4) The certification regulations of the Food and Drug Administration themselves permit variations of from 67 percent to 150 percent from the potency claimed on the label of the disk (21 CFR 147.1(f)). This is because such variations cannot be avoided. Obviously, therefore, with or without certification there will be variations in

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[10] Gould, *The Laboratory Control of Antibiotic Therapy*, 3 Chemotherapia 477, 478 (1961); World Health Organization Technical Report Series No. 210, *Standardization of Methods for Conducting Microbic Sensitivity Tests*, Second Report of the Expert Committee on Antibiotics (1961), 14-16; *Standardization of Methods for Conducting Microbic Sensitivity Tests*. Preliminary Report of a Working Group of the International Collaborative Study Sponsored by the World Health Organization (November, 1964), 23-25.

zone sizes between different disks containing the same antibiotic substance.

(5) If proper standards and controls are established for the conduct of sensitivity testing and for reading and reporting of results, the laboratory worker will not be misled by a faulty disk. If proper standards and controls are not established and followed he may be misled, with or without certification (I-B, *infra*). This does not mean, however, that the physician will be misled. The disk test result is only one of the many sources of information upon which he relies to form a clinical judgment.

(6) The Government creates the impression that sensitivity tests are routinely run by or on the order of physicians and that all or most antibiotic therapy is based on the results of such tests. This is not a fact. The record reveals with clarity that such tests involve a complicated procedure which can only be followed by trained technicians and that they are conducted in clinical laboratories, primarily hospital laboratories, *after* initial therapy has been begun.

Dr. Keefer said when asked whether it was "customary or rare" for practicing physicians to conduct sensitivity tests: "I would say from the total number of infections that doctors see and treat, both in their offices and in the home, and many in hospitals, the sensitivity test is not used. It is not used routinely". (App. 123).

According to Medical Market Guide (pp. 17, 60, 61)[11] the total sales of antibiotics in the United States in 1967, amounted to $375,175,000. Of this amount $286,631,000 or 77 percent, were purchased on prescription, or by physicians. Both Dr. Keefer's testimony and common experience teach that physicians treating patients outside hospitals do not routinely order sensitivity tests. One

[11] Modern Medicine Publications, 4015 W. 56th St., Minneapolis, Minnesota.

very good reason is that a test is ordinarily not necessary because the initial therapy with a wide spectrum antibiotic is likely to be effective. It is apparent, therefore, that the Government has exaggerated the extent of the use of sensitivity disks far beyond actuality.

B. *Some Improvident Statements in the Government's Brief*

(1) (a) ". . . it became important in medical practice to have a screening test which would provide the physician with an accurate estimate as to which among the several available antibiotics would be likely to be effective against his patient's infecting organism" (Pet. Br. 7).

(b) "Today, approximately 82 percent of the hospitals and clinical laboratories in the United States conduct sensitivity tests prior to the initiation of antibiotic therapy . . ." (Pet. Br. 19).

The quotation in (1) (a), above, implies that sensitivity testing is conducted *before* administration of an antibiotic. The quotation in 1(b) specifically states that this is done in some 82 percent of the hospitals and clinical laboratories in the United States. The first quotation is misleading. The second is untrue (See I-A(6), *supra*) and is not even supported by the Isenberg article cited.[12] The article states at page 186, that in almost 82 percent of "the institutions cultures are taken prior to the initiation of antibiotic therapy." It is perfectly clear that the author was referring to the 66 institutions which answered his questionnaire, not to all institutions in the United States. Moreover, it is obvious that taking a culture prior to the initiation of antibiotic therapy is not the same thing as conducting a sensitivity test. Cultures are taken for many purposes other than

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[12] Isenberg, *A Comparison of Nationwide Microbial Susceptibility Testing Using Standardized Discs*, 1 Health Laboratory Science 185, 186 (1964).

disk sensitivity tests. Moreover, as the testimony shows (*Infra* at II B) the usual order of procedure is (i) taking the culture, (ii) isolation of the organism, (iii) incubation of the isolate, (iv) the sensitivity testing procedure.

It is undisputed on the findings and record of the trial of this case, so studiously neglected in the Government brief, that initial therapy is "almost always" begun before the result of the sensitivity test is received by the physician from the laboratory (App. 143-144). The reason is obvious. The physician can not afford to await the result of a sensitivity test before instituting treatment of an infectious disease.

(2) It is said ". . . a patient's life may well be jeopardized by a disk which contains, *e.g.*, an excess in potency with too rapid diffusion, giving a false reading of sensitivity to that particular antibiotic." (Pet. Br. 21-22). The alleged false reading would, of course, be occasioned by a large zone size, if such a reading should occur. But such a result is remote indeed. It was understood as early as 1956 that "Because of differences in diffusibility, the zone sizes are different for virtually every one of the drugs . . . also, in reading the results it is important for the laboratory worker to understand that sensitivity to each antibiotic is to be considered separately. Once this simple point is grasped and the standards are followed closely, differences in zone sizes have led to no confusion." [13]

The reference in the above quotation to "the standards" is explained by the statements on page 892 and 896 of the article of Kirby et al. that "It is necessary of course, to have a different set of standards [of zone sizes]

[13] Kirby et al., *Clinical Usefulness of a Single Disc Method for Antibiotic Sensitivity Testing*, Antibiotics Annual, 1956-1957, 892 at 894.

for each chemotherapeutic agent, since there are variations in the degree of diffusibility". Standard control cultures of known sensitivity should be included in every test.[14] We have heretofore noted that the regulations of the Food and Drug Administration permit variations of from 67 percent to 150 percent from the potency claimed on the label of the disk (21 CFR 147.1(f)), because variations in the amount of chemical on the disk are unavoidable.

No laboratory technician, with or without certification of disks by the Food and Drug Administration, will know whether his system is operating satisfactorily so that he can detect abnormalities in test results unless he runs controls on his routine procedures. This is true of chemical analyses and serology generally as well as disk tests. Any good laboratory tests and uses cultures (strains) of known sensitivity which yield specific zone sizes under the particular conditions of the test as performed in that laboratory, as a basis for comparison with unknown strains.

The following things are therefore apparent: (a) that, with or without certification, there will be differences in zone sizes both between the various antibiotics (because of differences of diffusibility) and between different disks bearing the *same* antibiotic substance (because of the many variables in the testing procedure and the unavoidable variations in the quantity of the antibiotic substance); (b) that if the laboratory conducting the sensitivity test has not established standards, including that of anticipated zone size, the laboratory worker may be misled with or without certification and, conversely, if the proper controls are used, variations in zone sizes will not mislead him.

Obviously, therefore, an excess of potency would not mislead the adequately trained and properly prepared

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[14] Broadsheet No. 55, The Association of Clinical Pathologists, October, 1966, at 2 and 4.

laboratory technician.[15] He would be suspicious of the larger-than-usual zone size. If there were no zone at all, as was found in some of the tests described in Branch et al.,[16] the physician can simply use another antibiotic since, as Dr. Wolfe, a witness for the Government said at the trial, the physician always has a choice of more than one antibiotic (App. 74) and the test organisms taken from an ill patient are always run with seven or eight or more chemotherapeutic agents.[17] The Bacto-Unidisk itself carries eight such agents and an additional three or four may be placed in the center of the Unidisk.[18] As Kirby et al. said at page 894 (Note 13, *supra*), "... tube dilution tests may be indicated when readings fall in the middle zone or are borderline for other zones. In actual practice, that is rarely necessary." Or, as one authority cited in the Government's brief recommended, if there is no zone at all or if the zone is too large, repeat the test using three or more disks of the same strength.[19] Since in most cases the organism will already have been identified the repeat test can be done in some eight hours.

Moreover, it is essential to understand, as stated by Bauer[20] that "variations in content of high potency discs

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[15] The literature cited by the Government on page 21 of its brief is consistent with these statements.

[16] Branch, Starkey, Power, and Greenberg, *Problems of Standardization of Manufactured Dry Penicillin Sensitivity Disks*, Antibiotics Annual 1956-1957, p. 898 (Pet. Br., Note 19, p. 25).

[17] Bauer, *The Significance of Bacterial Inhibition Zone Diameters, A Study of the Factors Influencing Antibiotic Disc Sensitivity Tests*, Proceedings of Third International Congress of Chemotherapy 466 (1963).

[18] Labeling of Unidisk (App. 184).

[19] Rose and Berky, *A Quality Control System for Disk Antibiotic Testing*, 48 American Journal of Clinical Pathology 200, 203-204 (1967).

[20] Bauer, *supra* at 468.

have negligible influence on zones." This is also true of low potency disks.[21]

(3) It is stated in the Government's brief that "From the presence and size of the clear zones of inhibition around the various discs, the microbiologist is able to advise the physician which of the antibiotics have demonstrated the greatest effectiveness against the infecting microorganism." (Pet. Br. 8). This statement reflects, again, a misapprehension of the function of the disk testing procedure. The results of the tests are *in vitro* only. A reading of the publications cited in the Government's brief establishes beyond any doubt that there can be no such easy and complete translation of the results to *in vivo* effect as is suggested by the quotation and, indeed, as is implied throughout the brief. The physician must take many factors into consideration before using one of the antibiotics to which the test has indicated the microorganism is sensitive.

In the first place, since the patient will, in most cases, already be receiving initial therapy, the likelihood is that the test will merely confirm the physician's judgment (Finding of Fact No. 8, App. 194). Secondly, as stated by Petersdorf and Sherris: [22]

> "It should be clear, however, that the disc producing the largest zone of inhibition does not necessarily

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[21] The regulations of the Food and Drug Administration permit a variation of 2½ millimeters between the diameter of the largest and the smallest zone of a disk of a given labeled potency (21 CFR 147.1(f)). Based on the "standard curve" of potencies set forth in the regulations (21 CFR 147.1(d) this means that the difference between the lowest and highest potencies may be almost 250 percent. Moreover, in three or more consecutive tests 10 percent of the total number of disks tested may have zones which fall outside the prescribed range. In large batches of thousands of disks it seems obvious that the prescribed procedure is not very meaningful.

[22] *Methods and Significance of in Vitro Testing of Bacterial Sensitivity to Drugs*, 39 American Journal of Medicine 766 (1965).

indicate the antibiotic of choice for a given pathogen. For example, if a strain of Esch. coli shows a zone of 22 mm. around a 30 microgram tetracycline disc and a zone of 26 mm. around a 30 microgram chloramphenicol disc, all that can be said is that the strain is susceptible to both compounds. From the agents reported as being effective against the offending organism, the clinician can then select the one most appropriate for therapy. Pharmacologic and toxicologic properties as well as the bacteriostatic or bactericidal actions of the drugs should be considered in making this selection." (pp. 773-774).

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"As with the results of any other laboratory examination, in no case should the zone of inhibition around a paper disk be the sole criterion for selection of a chemotherapeutic, since many other factors must be considered" (p. 777).

These quotations are fair and correct statements. The exaggerated assertion in the Government's brief cannot be reconciled with them.

(4) The references to "potent anti-microbials" and the cautions that their use should be "accompanied by" or "in conjunction with" appropriate "culture and susceptibility" or "sensitivity" testing (Pet. Br. 22-23 and note 17) are entirely consistent with the facts as we have stated them, i.e. that the physician rarely waits for a sensitivity test result before commencing therapy. If he orders such a test at all, the testing procedure would proceed during the primary or initial therapy, as advised in Physicians Desk Reference for Lincocin (lincomycin) and in the prescribing directions of the Food and Drug Administration for chloramphenicol.

The real key to the otherwise portentous references to such drugs as chloramphenicol is the first sentence of the first full paragraph on page 22 of the brief which advises that ". . . the labeling for most of the antibiotics

listed in 21 CFR 145.3 . . . contains directions that the drug is to be used *against known sensitive organisms*, or *after* antibiotic sensitivity testing of the patient's organisms or bacteriologic tests of the sort provided by the sensitivity units." (Emphasis supplied). There are many "known sensitive" organisms as shown by Dr. Weinstein's table of "Current use of Antimicrobial Agents in the Therapy of Infections".[23] Moreover, ". . . the labeling for most of the antibiotics" does *not* as stated by the Government, recommend administration of the drug *after* sensitivity testing. Even in the case of the two examples cited (Lincocin and chloramphenicol) this is not recommended. The statement in question is obviously misleading.

Finally, it must be understood that an inadequate sensitivity test will not cause the physician to administer chloramphenicol. The test will almost always, if not always, show sensitivity of the organism to a number of antibiotics, of which as many as 15 or more may be used in the test. The careful physician will obviously not choose the most dangerous drug (such as chloramphenicol) if there are one or more others to which the organism is sensitive and certainly not if the patient is already responding to the initial therapy. Any prescribing of chloramphenicol without adequate justification, as reported in the press, has certainly not been done on the basis of sensitivity tests.

II.

The Bacto-Unidisk is not a "drug" Within the Meaning of Section 201(g)(1)(B) of the Act

The Government's chief legal argument (Pet. Br. 28 et seq.), in support of its contention that disks are drugs within the statutory definition is that such a construc-

[23] Goodman and Gilman, *supra*, at 1176 et seq.

tion would further the "statutory purpose" of ensuring the safety and efficacy of use of antibiotics and antibiotic sensitivity disks. Such a construction, it is said, would accord "with the settled principle that the Federal Food, Drug, and Cosmetic Act is properly given a broad construction in accord with its purpose to protect the public health" (Pet. Br. 32). The government cites decisions of this court which "emphasize" that "it is within 'the right and the wisdom' of Congress to provide its own glossary of terms and definitions in the Federal Food, Drug, and Cosmetic Act, and . . . the judicial function is to apply what the Congress has written" (Pet. Br. 32). It is also stated that "as the district court acknowledged", sensitivity disks fall within the literal definition of the term drug (Pet. Br. 29-31) and therefore should be construed as drugs to effectuate the statutory purpose. Petitioner concludes that the courts below erred by disregarding both the statutory definition of the term "drug" and the purpose of the statute.

A. *The Remedial Nature of the Statute and The Glossary of Definitions Contained Therein*

1. Congress did indeed provide its own glossary of terms and definitions and this court must apply them in this case.

The statute is concededly remedial and, in the appropriate case, its terms should be given a broad construction in accord with that remedial purpose.

The matter of the remedial purpose of the Act is in fact, however, inapposite to this case. "The courts below did not . . . dispute either the need or the desirability of batch testing of antibiotic discs" (Pet. Br. 28) for the simple reason that no probative evidence of any public health hazard was produced in the case. The only "evidence" was unsupported opinion. The two government witnesses who expressed an opinion were unable to cite

any instance of the wrong antibiotic being administered to a patient because of a sensitivity test using a faulty disk (App. 83-84, 93-94, 140-141), and a witness for Difco Laboratories, Inc. testified affirmatively that he knew of no such public health problem (App. 125-126). The Government was thus unable to convince the lower courts that any public health hazard was involved in sensitivity testing, and now for the first time in this court attempts to create one by a barrage of citations to scientific literature which are *dehors* the record. The literature in question is discussed, *supra*. It does not support the contention that sensitivity disks are "drugs", nor does it justify the Government's dire warnings of danger to the public health.

The Government did not cite *United States* v. *Consolidated Laboratories, et al.*, Civil Action No. 63-C-23, D. Ill., March 29, 1963, also involving sensitivity disks. In that case the Government, as here, attempted unsuccessfully to show danger to the public health and the court found:

> "13a. There is no evidence of injury to the public from the use of the multidisk" (CCH Food, Drug, Cosmetic Law Reporter, Transfer Binder 1963-1967, ¶ 80,030).

It is, therefore, quite clear that no principle of broad construction in the light of the remedial purposes of the statute would justify a decision that sensitivity disks are drugs. As Mr. Justice Frankfurter cautioned in the *Imitation Jam* case (*62 Cases of Jam* v. *United States*, 340 U.S. 593), which is cited by the Government (Pet. Br. 32) in support of its position:

> "In our anxiety to effectuate the congressional purpose of protecting the public, we must take care not to extend the scope of the statute beyond the point where Congress indicated it would stop." 340 U.S. at 600.

2. The Government in its brief announces for the first time that "the more substantial question in this case is how to draw the line between 'drug' as defined in section 201(g) and 'device' which is defined in . . . section 201(h)" (Pet. Br. 29). It would do so on the basis of its "remedial purpose" concept. Similarly, in *Imitation Jam*, *supra*, the question arose as to how to interpret two provisions of the statute, *viz.*, section 403(c) and section 403(g). Adoption of the Government's approach to the manner of distinguishing the two provisions in the instant case would, we submit, "extend the scope of the statute beyond the point where Congress indicated it would stop" (*Imitation Jam*, 340 U.S. at 600). We discuss below the question of whether the disks could be regarded as "devices".

In *Imitation Jam* the government charged that a product labeled "Delicious Brand Imitation Jam" purported to be fruit jam and was misbranded under Section 403 (g) because it did not conform to the ingredient requirements of the standard for that product promulgated under Section 401. The district court, however, held that the product purported to be only an imitation fruit jam in conformance with Section 403(c) and therefore was not misbranded. This court sustained the decision of the district court, holding, as indicated above, that the public health purpose of the statute should not result in an unwarranted distortion of congressional language. To have held the food misbranded the court would have had to determine "that a practice Congress authorized by Section 403(c) Congress impliedly prohibited by Section 403(g)." 340 U.S. at 600.

In the case at bar, the statute defines the terms "drug" and "device" in substantially identical language, as stated by the Government (Pet. Br. 29). Petitioner's outline of the legislative development of the term "drug," and its treatment of the definitions, however, contain a substan-

tive omission. Petitioner states: "Senator Copeland . . . proposed an amendment to add a definition of 'device', parallel to that for 'drug', *but the drug definition was unchanged except for that revision.*" (Pet. Br. 34, emphasis supplied). The emphasized language is not correct; the definition of drug was subsequently revised in S. 5, 75th Cong., 3d Sess., April 14, 1938 (S. Rep. No. 2139) by the addition of the following language at the end of the definition: ". . . but does not include devices or their components, parts, or accessories." The drug definition *was* thereafter unchanged except for that revision.

The Government's brief ignores this excepting clause; *e. g.*, in a footnote on page 31, petitioner states that the Canadian Food and Drug Act "defines 'drug' and 'device' in language similar to that involved in this case." In fact, the pertinent portions of the Canadian definition of "drug" and "device," relating to diagnosis and treatment, are identical. The important factor is the absence in the Canadian law of a clause excepting devices from the definition of drug. The point is a significant one. Without the excepting clause an article could be both a device and a drug if its intended use fell within the statutory criteria. Thus, if sensitivity disks were intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, they could be classified as both drugs and devices and the Government would not be placed in the awkward position of attempting to ignore the fact that Section 201(g)(1) excepts devices from the definition of drug.

It should be noted that of the four basic jurisdictional definitions (foods, drugs, devices and cosmetics) in the statute, only that for drugs excludes other articles (devices) from its operation (the exclusion of soap from the definition of "cosmetic" is obviously not here pertinent). For example, articles may be and frequently are classified under the Act as both foods and drugs or as cosmetics and drugs depending upon the

representations made for them. See, *e.g.*, 33 F. R. 9352, where the Food and Drug Administration classified certain salt substitutes as both foods and drugs under the Act. It must be presumed that Congress in excepting devices from the drug definition did not engage in an idle act.

If, therefore, the court should adopt the Government's approach it would in effect be repealing that part of Section 201(g)(1) which excepts devices from the drug definition, and "extending the scope of . . . [of that provision] beyond the point where Congress indicated it would stop" (*Imitation Jam*, 340 U.S. at 600). This result would be analogous to that which would have occurred had the Court adopted the position urged by the Government in *Imitation Jam*, i.e., when the Food and Drug Administration has promulgated a definition and standard of identity for a food under Section 403(g), Section 403(c) is thereby deprived of any legal effect.

3. The Government urges as an approach to the problem of drawing the line (Pet. Br. 29) between drug and device, that adopted by the Court in *AMP, Inc.* v. *Gardner*, 389 F. 2d 825, cert. denied sub nom. *Amp, Inc.* v. *Cohen*, No. 86, this term, October 14, 1968,[24] i.e., to apply the Act "functionally to afford the public the protections of the statute" (Pet. Br. 33), and to reject "the idea that this important public law is 'restricted to products commonly called 'drugs'" (Pet. Br. 32). We show in Part II B, *infra*, that the action of the lower courts in this case in resorting to medical testimony to elucidate the meaning of the language in the statutory definitions was an approach which was proper and in accord with well-known principles of statutory interpretation enunciated by this Court. The AMP approach as interpreted by

[24] See discussion, *infra* Part II D.

the Government [25] would result in application of the definition of drug to any article, including devices, where, in the opinion of the Food and Drug Administration, the more restrictive requirements of the statute relating to drugs, new drugs and antibiotic drugs would protect the public. This is neither an orderly nor a legally justifiable way of determining the coverage of a statute. It ignores the exclusivity of the definition of drug in Section 201 (g) (1). It offers no standard for determining the delimitations of the definition of drug.

An even more basic evil lurks in the Government's interpretation of the *AMP* approach to the distinction between drug and device. The Federal Food, Drug, and Cosmetic Act is a stark, liability-without-fault, criminal statute.[26] As stated by Mr. Justice Frankfurter in *Dotterweich*,[27] a case involving criminal prosecution of a corporation president for violation of the Act:

> "The prosecution to which Dotterweich was subjected is based on a now familiar type of legislation whereby penalties serve as effective means of regulation. Such legislation dispenses with the conventional requirement for criminal conduct—awareness of some wrongdoing. . . . Hardship there doubtless may be under a statute which thus penalizes the transaction though consciousness of wrongdoing be totally wanting." (320 U.S. at 280-281, 284).

The Government in effect would have this Court lay down the following "standard" by which a businessman,

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[25] It is not necessary for this Court to adopt the vague, open-end approach urged by the Government as the basis for the result in *AMP*. As indicated in Part IID, *infra*, the article involved in AMP is composed of a material recognized as a drug in the United States Pharmacopeia, and therefore is arguably a drug under the statute (Section 201 (g) (1) (A)).

[26] Section 303.

[27] *United States* v. *Dotterweich*, 320 U.S. 277; see also *United States* v. *Wiesenfeld Warehouse Company*, 376 U.S. 86, 91.

at the risk of criminal prosecution if he be wrong, must determine whether his product is a drug or device: whether the statutory purposes of protecting the public would be served by his classification of the product. In order to make this determination, the businessman would have to resolve two questions: (1) whether in his opinion based on his knowledge of the product, the statutory purpose of protecting the public would be served by his decision; and (2) whether the Food and Drug Administration would agree with that decision. If he decides the product is a device and thereafter proceeds with production and the Food and Drug Administration concludes that the product is a drug, he may be subjected to criminal prosecution on at least five counts [28] and, if convicted, to imprisonment for five years or a fine of $5000 or both such imprisonment and fine (21 USC 333(a)). This result could follow regardless of any "consciousness of wrongdoing", as noted above.[29]

It is submitted that the *AMP* approach as interpreted by the Government (Pet. Br. 32-33) would result in an unconstitutionally vague application of the statute which would not enable a person subject to its terms to determine in advance whether his conduct will be considered criminal. As stated by this Court in a case in which defendant had been charged with evading the provisions of a price regulation promulgated by the Price Administrator pursuant to the Emergency Price Control Act of 1942, the law "must adequately inform those who are subject to . . . [it] what conduct will be considered evasive so as to bring the criminal penalties of the Act into

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[28] Section 301(d), (f), (p) and Section 301(a) based on various adulteration or misbranding charges in violation of Sections 501 and 502.

[29] In case of a violation with intent to defraud or mislead, the penalty could be imprisonment for three years or a fine of $10,000, or both such imprisonment and fine.

operation. . . . The dividing line between unlawful evasion and lawful action cannot be left to conjecture. The elements of evasive conduct should be so clearly expressed . . . that the ordinary person can know in advance how to avoid an unlawful course of action." *M. Kraus and Bros. Inc.* v. *United States*, 327 U.S. 614, 621-622 (1946).

In the instant case a person subject to the Act must know how to distinguish a drug from a device on the basis of substantially identical statutory definitions of those terms, i.e., is the article intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease. The only differences between the two definitions, insofar as here pertinent, are that Section 201(g)(1) excludes devices from the definition of drug, and Section 201(h) defines "device" in terms of instruments, apparatus and contrivances. As indicated above, the approach in *AMP*, as interpreted by petitioner, would in effect expunge these two differences from the definitions, with the result that the definitions would provide no clue whatever as to the meaning of drug and device. It is submitted that the distinction between drug and device would under the government's approach be "left to conjecture" and this criminal statute with its severe sanctions can not be constitutionally so applied. The same considerations are not present when the question to be determined is whether an article is a food or a drug or a cosmetic or a drug since the definitions of food, drug, and cosmetic do not contain such substantially similar language as do the definitions of drug and device.

B. *The Statutory Definition of "Drug" as Applied by the Lower Courts*

1. It is stated in the Government's brief (p. 29) that despite a contrary suggestion by the court of appeals, the disks fall within the literal definition of drug as articles intended for use in the diagnosis, cure, mitigation, treat-

ment or prevention of disease. The statement will not stand examination. It is beyond cavil that the word "treatment" as used in Section 201(g)(1)(B) means "treatment of a patient". It seems quite obvious that a disk used only as part of a test procedure in a laboratory is not used in the treatment of a patient.

The Court of Appeals held that the Bacto-Unidisk "has nothing to do with diagnosis or prevention of disease"; that "it is not intended for use either internally or externally to cure, mitigate, or treat disease"; and that "it only aids the physician to determine what antibiotics to use for the cure, mitigation or treatment of disease" (App. 200).

This is in accordance with the evidence. It is clear that the *information* obtained from the *sensitivity test* (not just from the disk) is used as a guideline to treatment of some cases of disease (App. 48, 56, 99, 104). The testimony fully supports the statement in Finding of Fact Number 8 (App. 194) that: "The information obtained from the sensitivity testing procedure outlined in Finding Number 7 is used by the physician as a guideline to treatment of the patient . . ."

No witness would accede to the Government's suggestions that the disk itself was used, or intended for use, in treatment, and the Government has abandoned that approach in this Court (Pet. Br. 29). Instead it states that "as a result of information as to the inhibiting action of the particular drug on the patient's particular infectious micro-organisms, the infection is diagnosed as one sensitive to a particular antibiotic, and the patient is treated with that particular drug" (Pet. Br. 29). This statement, however, is fraught with error. It implies that before treating a particular patient with a particular antibiotic for a particular infection, the physician awaits the results of a sensitivity test to see what antibiotic will inhibit the particular organism. The practice

of physicians is to the contrary, as all witnesses agreed (App. 60-61; 120-123; 143-144; Finding of Fact Number 8, App. 194). It is absurd to say that the infection is "diagnosed" as sensitive. The term diagnosis, as noted by petitioner (Pet. Br. 30) is a statutory term of art, and the statute speaks of *diagnosis of disease*, not diagnosis of the susceptibility of a pathogen to a drug.

"Diagnosis", Dr. Keefer testified, "is the recognition of disease or illness. That is the general medical term or interpretation of the term—recognition, identification of illness. . ." (App. 118). The disease cannot be recognized (diagnosed) until the suspected organism has been identified and "the disk does not enable one to identify an organism" (App. 118). Where the disk test is used, the first step is the identification of the organism; the second is the disk test. Dr. Keefer was asked: "If you skip that step, Doctor, [identification] and went right to the disk test, could you make a diagnosis?" He answered: "Could not make a diagnosis" (App. 119).

Finding of Fact Number 7 (App. 193) plainly states that the step of identification of the organism is preliminary to the sensitivity testing procedure. This finding also describes the information yielded by the test, i.e., an indication of whether the test organism is sensitive or resistant to the chemical on the disk. It is not logical to consider that information as a part of diagnosis or recognition of a disease condition. It is suggestive of the kind of treatment which may be appropriate but it is not suggestive of what disease condition is involved. The testimony lends no support to the contention that the disk is used in diagnosis.

Moreover, Finding of Fact Number 8 (App. 194) makes it clear, with respect to the information obtained from the sensitivity test that: "The disk, the culture medium, the Petri plate, and the incubation are all a part of the testing procedure yielding this information"; that "such in-

formation could not be obtained from the disk itself"; and that "the test is only one of many sources (such as the physician's experience, clinical symptoms, the literature, and other tests such as urinalysis and blood serum tests) of the information upon which the physician relies in determining the treatment to be administered". It is thus apparent that if the disk is a "drug", so are the culture medium, the Petri plate, and the incubator, as well as the medical literature and materials used in other tests such as urinalysis and blood serum tests (and others employing body specimens).

The District Court found that—

> "In medical science those substances which are for administration to or for use on, a person for the treatment of disease or injury, are regarded as drugs (Tr. 102-103, 195, 199, 261-262, 283). This is the commonly accepted view of physicians generally. A physician who testified for the libelant could think of no example of a substance not taken into or applied to the body which he would 'consider medically' as a drug (Tr. 103)". (Finding Number 9, App. 194).

The Court also found that "The article does not purport to be and is not represented as a 'drug' as that term is used in medical science or by physicians generally. It is labeled 'For Laboratory Use . . .'". (Finding of Fact Number 11, App. 195).

These findings are fully supported by the record and are not challenged by the Government. They lend powerful support to the clear purport of the testimony that the disk is not used in the diagnosis or treatment of disease.[30]

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[30] The definition of "drug" in Dorland (Pet. Br. 30, Note 27) is plainly limited to substances "for the relief of pain or suffering, or to control or improve any physiological or pathological condition." All of the preceding portions of the definition are modified by the portions quoted. Moreover, Stedmans Medical Dictionary (21st Ed. 1966), Blakiston's New Gould Dictionary (2nd Ed. 1956), Butterworth's Medical Dictionary (1965), and Webster's New International Dictionary, all define "drug" as a medicine. This is entirely consistent with Dorland.

The Bacto-Unidisk is a laboratory reagent. There are more than 150 pages in the United States Pharmacopeia (and others in the National Formulary) describing hundreds of laboratory reagents or testing materials for use in making the various tests and assays described in the Pharmacopeia.[31] If the Government's position that sensitivity disks are used in the treatment of disease or in the diagnosis of an infection were sound, the Food and Drug Administration could, on the basis of the same approach, classify many, and perhaps most, of those reagents as "drugs" under the statute.

There is absolutely no warrant for the extension of jurisdiction over these laboratory tools, either in the statute or its legislative history. The proper forum for the Administration to advocate the subjection of sensitivity disks to the Act is the Congress. If the Administration can present a serious basis for statutory coverage of disks it will, as it has heretofore, receive the attention of the national legislature. Instead, during the six years of this litigation, the spectre of danger to health has been repeatedly flaunted without the production of any data to support it.

If the Government's position were sound the disk could legally be represented in its labeling as suitable for the treatment of disease; for example, "for use in the treatment of bacterial infections." Such a statement would obviously be false and would constitute misbranding under Section 502(a) of the Act, under which a drug is deemed to be misbranded "if its labeling is false or misleading in any particular."

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[31] These reagents are not regarded as drugs by the Committees on Revision of the official compendia (Sec. 201(j), 21 U.S.C. 321 (j)) and therefore do not appear in the monograph section of the compendia. Thus, they are not "recognized" in the sense of Sec. 201(g)(1)(A). (App. 153-154; 155-157; 167-171).

2. The Courts below were not in error, as suggested by petitioner (Pet. Br. 32) in "their application of . . . the common medical usage of the term drug" to the statutory definition of that term. The statute does contain its own definition of "drug", thereby making that word a term of art (Pet. Br. 30). The applicable portion of the definition is, however, composed of words having a technical meaning, i.e., "diagnosis, cure, mitigation, treatment or prevention of disease." Recognizing this fact, *both petitioner and respondent* presented evidence by medical and scientific witnesses as to the meaning of the word "drug" in terms of the statutory definition, and its application to sensitivity disks, and specifically as to the meaning of the terms "diagnosis" and "treatment". In receiving such evidence, the trial court was following a long-established principle of statutory construction set forth by this Court in a number of cases, *viz.*, resort to expert evidence *aliunde* in order to give meaning to technical statutory language. *Binns et al.* v. *Lawrence*, 53 U.S. 9; *Boston Sand & Gravel Co.* v. *United States*, 278 U.S. 41; *National Labor Relations Board* v. *Coca-Cola Bottling Co.*, 350 U.S. 264. If terms such as "diagnosis" and "treatment" are not to be given the meanings ascribed to them by physicians, where, as here, no legislative history explains them, the courts are left with no expert advice on the matter at all.

Petitioner agreed at the trial that the experts were of help to the Court in this matter (App. 105). Petitioner cannot now ignore the testimony of its witnesses and respondent's as to the meaning of the terms "diagnosis" and "treatment" and the word "drug". Even if the finding of the District Court that the term "drug" is limited to substances administered or applied to patients were entirely ignored, we submit that the evidence shows that the disks are nevertheless not "drugs" because they are not used in "diagnosis" or "treatment", as the testimony and findings show.

Securities and Exchange Commission v. *Ralston Purina Co.*, 346 U.S. 119 (Pet. Br. 29-31) is inapposite. There, the offering of securities with respect to which no registration statement was in effect was clearly within the statutory prohibition *unless* it was exempt as "not involving any public offering". The Court, following established principles, placed upon the issuer of the securities the burden of proof of showing that the offering fell within the exemption. The issuer was unable to meet the burden. Here, in contrast, the burden of proof was upon the government to establish that Bacto-Unidisks were "drugs". It failed to do this and now offers its frail public health argument as a basis for overturning the findings and decisions of the lower courts.

C. *The Memorandum Opinion of the District Court*

The Government makes the statement, and relies upon it, that the district court ". . . acknowledged (App. 190) that the discs fall within the literal definition of 'drug' in Section 201(g) . . ." (Pet. Br. 29, 30, 33).

It is clear, however, as shown above that it is not the disk (the "article" seized) but the *information* obtained from the sensitivity testing procedure as a whole, which is used as a guideline to therapy, and that such information does not in any sense constitute a "diagnosis" of the patient's infection.

It is well-established, moreover, by decisions of this Court, that an appellate court may not refer to a memorandum opinion of a District Court sitting without a jury, for the purpose of impeaching that court's formal findings of fact; or, as this Court stated it "for the purpose of eking out, controlling, or modifying" such findings. *Stone* v. *United States*, 164 U.S. 380, 383 (1896); *Saltonstall* v. *Birtwell*, 150 U.S. 417 (1893); *United States* v. *Shoshone Tribe of Indians*, 304 U.S. 111, 115 (1938); *M. E. Blatt Co.* v. *United States*, 305 U.S. 267, 277

(1938). Where no part of the memorandum opinion is regarded by the trial court as a finding of fact, statements contained therein cannot be utilized on appeal to refute or negate findings of fact expressly made by the court. *General Metals Powder Co.* v. *S. K. Wellman Co.*, 157 F.2d 505, 509, cert. denied 329 U.S. 812, rehearing denied 330 U.S. 854.

It seems perfectly clear in the instant case that the trial court's memorandum opinion did not and was not intended to contain findings of fact. On the contrary, the court invited the parties to submit findings of fact and conclusions of law. The subsequent adoption by the court of detailed formal findings of fact and conclusions of law after proposed findings and conclusions were submitted by counsel is conclusive evidence of the court's intention with respect to the memorandum opinion and brings the case within the above-cited case authorities.

Moreover, an appellate court may not set aside the findings of fact of the trial court unless they are found to be "clearly erroneous". They are not clearly erroneous unless the reviewing court, on the entire evidence, is left with the definite and firm conviction that a mistake was committed. *United States* v. *United States Gypsum Co.*, 333 U.S. 364, 395, rehearing denied 333 U.S. 869 (1948); *Commissioner of Internal Revenue* v. *Duberstein*, 363 U.S. 278, 291 (1960); *S. C. Johnson & Son, Inc.*, v. *Johnson*, 266 F. 2d 129, 142-143 (6th Cir., 1959), cert. denied, 361 U.S. 820. It is not enough that the appellate court might give the facts another construction or resolve the ambiguities differently. *United States* v. *National Association of Real Estate Boards*, 339 U.S. 485, 495-496 (1950).

The burden of proof is upon the Government to prove to the appellate court that the trial court's findings and conclusions are clearly erroneous, *S. C. Johnson & Son, Inc.* v. *Johnson, supra*, at 143

In a recent decision the Court of Appeals for the Sixth Circuit emphasized that Rule 52(a) is not a purely arbitrary rule but a well-established, frequently applied, principle of law. *Krumholz* v. *Good*, 318 F. 2d 911, 912 (6th Cir. 1963).

The Government in its brief in the court of appeals and here has largely ignored the formal findings of fact and conclusions of law of the District Court and has made no effort to sustain its burden of proving that the trial court's findings and conclusions are clearly erroneous as required by *Johnson, supra.*

Obviously, therefore, the Government may not undercut the court's formal findings of fact by use of a statement in the Memorandum Opinion. Moreover, in the formal conclusions of law of the court (Number 4, App. 196) it is stated that —

> "The seized article does not purport to be nor is it represented to be a drug within the meaning of 21 U.S.C. 321(g). It is not intended for drug use (See Findings Numbers 9 and 10) and it is the intended use which determines its status under that Section . . ."

D. *AMP, Inc.* v. *Gardner*

As above indicated, petitioner urges that this court in distinguishing between drug and device adopt the government's interpretation of the approach taken in *AMP, supra, viz.*, that the statute should be "applied functionally to afford the public the protections of the statute" (Pet. Br. 33) and is "not restricted to products commonly called 'drugs'" (Pet. Br. 32). *Bradley* v. *United States*, 264 Fed. 79, is also cited to support the latter point.

The purpose of noting that the Act is not restricted to products commonly called drugs or to dictionary or pharmacopeia definitions is obscure, since nobody to our knowledge disputes the proposition that it is the "intended

use" of the product which determines whether it is a drug (i.e., whether it is for use in the diagnosis or treatment of disease) and the Court of Appeals specifically recognized that principle in the instant case (App. 201). That is why spring water is a "drug" if it is recommended for use in the treatment of disease. *(Bradley* v. *United States, supra).* Obviously therefore we do not urge and the court below did not hold, that the Act is restricted to products commonly called drugs. The effect of the decisions below was that, since the Bacto-Unidisk was neither held out for the diagnosis or treatment of disease nor used in or on the body it was not a "drug" under the statute.

In its Brief in Opposition to the Petition for Certiorari in *AMP* the Government states with respect to the suture material there involved (p. 7):

> "The essential element, nylon suture material, is recognized as a drug in the official United States Pharmacopeia and therefore is squarely within that portion of the statutory definition which defines as drugs 'articles recognized in the Official United States Pharmacopeia.' Cf. *United States* v. *48 Dozen Packages . . . of Gauze Bandage,* 94 F. 2d 641 (C.A. 2)".[22]

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[22] Section 201(g), the definition of "drug", is composed of three clauses: Clauses (A) defines drug in specific terms, *viz.*, articles recognized in the official compendia; clauses (B) and (C) define drug in general language which would include the drugs in the compendia, *viz.*, articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease, or intended to affect the structure or function of the body. It is submitted that due to the manner in which the term is defined in the statute, the rule of *ejusdem generis* is applicable. Under that rule, sensitivity disks would not be considered drugs since they are not recognized in the official compendia, and are not "of a kind with" articles which are recognized in the compendia. See *United States* v. *48 Dozen Packages . . . of Gauze Bandage,* 94 F. 2d 641 (2d Cir. 1938). Judge Thornton found as a fact that based on the testimony adduced at the trial, disks are not the kind of articles which are accepted for admission to the official compendia (Finding No. 9, App. 194).

Moreover, the Brief in Opposition in *AMP* (pp. 8-9) notes that, unlike the disks, the article there involved enters the surgical wound and part of it remains in the body. It also points out (p. 7) that the article is used to ligate or tie off bleeding blood vessels during a surgical operation and that, therefore, it affects the structure or function of the body within the meaning of Section 201 (g) (1) (C).

It is fully apparent therefore that there are both legal and factual differences between the instant case and *AMP*, and the Government so states in its Brief in Opposition in *AMP* (pp. 8-9). Even more conclusive, however, is the fact that the manufacturer of the product in AMP, unlike Difco Laboratories, did not dispute the proposition that its product was subject to the Act (either as a drug or as a device) and, in the language of the court of appeals, "proceeded to comply with the requirements of the Act relating to devices" (389 F.2d at 826).

It was conceded, therefore, that the product in AMP was "intended for use in the diagnosis, cure, mitigation or treatment of disease" or "intended to affect the structure or function of the body", or both, since it would not be a device under Section 201 (h) unless it was intended for one of more of such uses. The language relating to diagnosis and treatment (Section 201 (h) (1)) and that relating to affect upon the structure or function of the body (Section 201 (h) (2)) are common to the definitions of "drug" and "device". The very question in the Bacto-Unidisk case is whether the disk falls within the provision of Section 201 (g) (1) which corresponds to Section 201 (h) (1), *viz.*, Section 201 (g) (1) (B), relating to diagnosis and treatment.

It is obvious, therefore, that the "broad construction" given to the Act in *AMP* is not comparable to that which the Government is seeking with respect to Bacto-Unidisks.

In the former the basic jurisdictional test was concededly met and the question was only one of classification as between "drug" and "device". In the latter the testimony at the trial shows that the basic jurisdictional test, *viz.*, whether the disk is used in the diagnosis or treatment of disease, is not met. In addition, the possible dangers involved in incorporation of a substance into the human body are obviously not present in the case at bar.

III.

The Certification Provision (Section 507) is Not Applicable to Articles Not Administered or Applied to Patients.

It is stated by the Government that the only substantive question in the case is whether the Bacto-Unidisk is a "drug" (Pet. Br. 10). This is not correct. We have consistently pointed out that, even if the article were held to be for use in the "diagnosis" or "treatment" of disease and therefore held to be a "drug" under Section 201(g)(1)(B), it is not for administration or application to patients and therefore is clearly not subject to certification under Section 507. This is clear from the legislative history of Section 507 which is recited in part in the Government's brief.

The Government fails to point out that (1) when section 507 was enacted in 1945 no sensitivity disks were being produced commercially and Congress had never heard of such articles, (2) the language of section 507 and portions of the legislative history unmentioned by the Government clearly show that the concern of the Food and Drug Administration and Congress was to protect patients from the administration of an antibiotic drug (penicillin) which was not safe and efficacious for such administration without stringent controls.[33] This purpose

[33] S. Rep. No. 410 and H.R. Rep. No. 702, 79th Cong., 1st Sess. (1945).

—to protect patients receiving antibiotic drugs—was not changed in 1947, 1949, or 1961.[34]

The quotation from the testimony of Secretary Ribicoff (Pet. Br. 16-17) is obviously applicable only to antibiotics administered to patients. The phrase "Since they are employed in conditions where even minor delays in effective treatment may result in death . . ." used by the Secretary could not be applicable to sensitivity disks by any reasonable interpretation since, by its very nature, the disk test involves substantial delay.

In a letter to the President of the Senate the Federal Security Administrator[35] said that the drugs being added to the certifiable list in 1949 were "highly efficacious for one or more serious diseases", such as rickettsial diseases, atypical pneumonia, and virus diseases.[36] Obviously the Administrator was talking about drugs to be used for administration to patients.

In 1962 Section 507 was amended to extend certification to all antibiotics "intended for use by man" (as distinguished from veterinary use).[37]

The words "intended for use by man" and "for human use" are used interchangeably throughout the several committee reports on the bills which became the Drug Amend-

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[34] *E.g.*, S. Rep. No. 600, 81st Cong., 1st Sess. (1949), 1949 U.S. Code Congressional Service 1530-1531.

[35] The predecessor of the Secretary of Health, Education and Welfare.

[36] Op. cit. supra., S. Rep. No. 600, U.S. Code Congressional Service at 1531, 1532.

[37] Drug Amendments of 1962, P.L. 87-781, 76 Stat. 780, Sec. 105 (a), amending Section 507(a).

ments of 1962.[38] In the context, they quite clearly refer to use for administration to man by ingestion or otherwise. Thus, the uses of sensitivity disks are clearly excluded, whether the organism being tested by the disk is from man or animal.

The Department or Health, Education and Welfare, under date of October 10, 1962, released a document entitled, "Drug Amendments of 1962, Federal Food, Drug and Cosmetic Act—Summary", which is explicit. It states under "Batch Certification of Antibiotics" that:

> "14. All antibiotic drugs to be *administered to humans* are made subject to batch-by-batch testing and certification by FDA for identity, strength, quality, and purity to assure that they "are safe and effective before they are released for sale." [Emphasis supplied].[39]

Sensitivity disks, of course, are not "administered" at all. It is evident, therefore, that the Congress, in extending certification authority in the 1962 amendments, and limiting it to antibiotics administered to human beings, was following the pattern established by Section 507 as originally enacted and as reflected in its legislative history.

Moreover, it seems quite clear that the concept of "safety of use" is applicable only to dosage forms of substances which are administered to patients. This is the clear pattern of the statute. Thus, "safety of use" is a statutory test of pre-marketing clearance of a "new drug" under Section 505 of the Act. It clearly refers

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[38] S. Rep. No. 1744, Parts I (July 19, 1962) and 2 (August 21, 1962), 87th Cong. 2d Sess., on S. 1552, p. 19 (Part I) and p. 9 (Part 2); H.R. Rep. No. 2464, 87th Cong., 2nd Sess., p. 11 (1962); H.R. Conference Report No. 2526, 87th Cong., 2d Sess., on S. 1552, p. 21 (1962). Part I of the Senate Report and the Conference Report are set out in U.S. Code Congressional and Administrative News, Vol. 2, 1962, at pp. 2884 and 2927.

[39] A subsequently issued printed pamphlet entitled "Summary of the Drug Amendments of 1962" repeats this statement on page 6.

to safety for application or administration to patients.[40]

The concept of safety of use is inapplicable to sensitivity disks, since they are not applied or administered to the patient. It seems clear, therefore, that, even if they were drugs, they would not be subject to certification under Sec. 507.

The same is true of one of the most important of the original provisions of the statute, Section 502(j), under which a drug is deemed to be misbranded "if it is dangerous to health when used in the dosage or with the frequency or duration prescribed, recommended or suggested in the labeling thereof". This provision patently applies to drugs in dosage forms for administration to individuals and not to laboratory reagents such as sensitivity disks.

It seems apparent therefore that even if the sensitivity disks were drugs, they would not be the kind of drugs which are subject to certification.

IV.

If the Bacto-Unidisk Were Subject to the Federal Food, Drug, and Cosmetic Act it Should be Classified as a Device

The suggestion was offered to the lower courts on behalf of respondent that, if the Bacto-Unidisk were subject to the Act at all (respondent contends it is not), it should be treated as a device within the meaning of Sec. 201(h). As a device it would not be certifiable.

The only difference between a drug and a device insofar as the definition of "device" and the pertinent por-

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[40] See, e.g., Report of Special Committee to Review the Policies, Procedures, and Decisions of the Division of Antibiotics and the New Drug Branch of the Food and Drug Administration (approved September 27, 1960); and analysis of H.R. 11581, 87th Cong., 2d Sess., by Department of Health, Education and Welfare, Hearings before the Committee on Interstate and Foreign Commerce, House of Representatives, 87th Cong., 2d Sess., on H.R. 11581 and H.R. 11582 (p. 23).

tion of the definition of "drug" (Section 201(g) (1) (B)), are concerned, is that devices are "instruments, apparatus and contrivances" and drugs are articles other than instruments, apparatus, and contrivances.[41]

Sensitivity disks are logically classified as "instruments, apparatus, or contrivances, "if they could be regarded as used in the "diagnosis" or "treatment" of disease. As the testimony shows, there is nothing in the nature or manner of use of reagent disks to justify a holding that they are used in "diagnosis" or "treatment" and, of course, they are not used in or on the body. They therefore logically fall neither within the definition of "drug" nor that of "device". It is, however, somewhat less difficult to conceive of them as "devices" because they are in fact a "means" or "appliance" within the dictionary definition of the term.[42]

A "generator" supplying chlorine gas for *inhalation* by patients to treat arthritis and sinusitis was considered by the Food and Drug Administration and treated by the Court as a "device" in *United States* v. *22 Devices . . . Halox Therapeutic Generator*, 98 F. Supp. 914 (D. Cal. 1951).

A so-called cancer diagnosis kit with two bottles of common chemicals (one of which was ether, a substance commonly used as a drug), which were to be added to a sample of the patients urine to determine whether cancer

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[41] The last clause of Section 201(g) (1) expressly provides that the definition of "drug" does not include devices.

[42] The pertinent definitions in Webster's New International Dictionary are as follows: Device: "1. That which is devised, or formed by design; a contrivance; an invention. . ." Instrument: "1. That by means of which any work is performed or result is effected; a medium; means." Apparatus: ". . . Specif. Any complex instrument or appliance, mechanical or chemical, for a specific action or operation. . ." Contrivance: ". . . 3. A mechanical device; an appliance."

was present, was considered to be a "device" and an injunction was granted against its shipment.[43] Likewise, a radio diagnostic and treatment machine which was held forth as requiring only a drop of the patient's blood for diagnosis and treatment of various disease conditions, was considered by FDA as a "device", not a drug. The device was seized and a criminal prosecution was brought against its shipper.[44]

It seems manifest that if the disks are drugs because their use involves the testing of organisms from the patient as an aid in deciding upon the proper treatment, the last two devices above described likewise fall into that category. In fact, however, it seems clear that none of the three articles is a drug.

The World Health Organization Technical Report Series No. 210, cited in the Government's brief (p. 21) states, at page 13 that "It is desirable that each government should ensure some system of control over the quality and particularly the antibiotic content of such commercially prepared discs" and that "It is necessary that batches from each manufacturer should be tested from time to time . . ." To the same effect is the Government's brief, pp. 20-21.[45]

We have above noted that, if sensitivity disks are subject to the Federal Food, Drug, and Cosmetic Act, they must fall within the definition of "device" in Section

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[43] Annual Report of the Food and Drug Administration, 1953, Kleinfeld & Dunn, Federal Food, Drug and Cosmetic Act, 1953-1957, p. 650.

[44] Annual Report, Food and Drug Administration, 1950, Kleinfeld & Dunn, Federal Food, Drug and Cosmetic Act, 1953-1957, pp. 575, 624.

[45] The brief implies that a dessicant is required by regulation. The regulations do not, however, require the use of a dessicant (21 CFR 147.2(b)). They leave it to the manufacturer to decide whether it is needed.

201(h). If, contrary to our view the disks are regarded as devices they could be subjected, as suggested by the Technical Report, to "some system of control" under the provisions of Sections 501 and 502 relating to the adulteration and misbranding of devices. A disk would be adulterated under Section 501(c) " if it did not contain the amount of antibiotic substance stated on the label. Thus, if the claimed potency of tetracycline were 10 micrograms and only 2 micrograms were present, the disk would be adulterated. Likewise, it would be misbranded under Section 502(a). The labeling would also have to bear adequate directions for use under Section 502(f).

Under its inspection and sampling programs the Food and Drug Administration could, as the Technical Report suggests, test batches of each manufacturer's disks "from time to time".

It is stated in the brief for the Government that there is need for an expiration date on the label of the disks. This matter could readily be handled under Section 201(n) of the Act. There can be no reasonable doubt that manufacturers of disks would comply if they were advised by the Food and Drug Administration that representation in the labeling of the amount of antibiotic in a disk would be misleading unless the labeling stated an expiration date because it "fails to reveal facts material in the light of such representations [as to potency of antibiotic substance] or material with respect to consequences which may result from the use of the article to which the labeling relates under the conditions of use prescribed in the labeling thereof" . . ." (Section 201(n)).

We have referred to the built-in protections against the possibility of erroneous information from a sensitivity test resulting in harm to a patient in the absence of any government control. There need be no apprehension to-

day that manufacturers would fail to label disks with an expiration date if there were no controls whatever. Manufacturers know that the laboratories which use disks want an expiration date and could not avoid including it in the labeling even if they were minded to do so. It is emphasized, however, that sensitivity disks are used neither to diagnose a disease nor to treat or prevent it. The information derived from them is at most an aid in determining whether the initial therapy should be continued. The disks are therefore distinguishable even from the alleged uses of the devices which have been described.

V.

The Legal Conclusion of the Commissioner of Food and Drugs that Sensitivity Disks are "Drugs" is Subject to Attack in this Proceeding

The Government in its brief states that it does not challenge respondent's right to question in a libel for condemnation proceeding, the legality of the determination of the Commissioner of Food and Drugs that antibiotic sensitivity disks are drugs (Pet. Br. 10). It does, however, point out that respondent did not seek "judicial review of the promulgating order as authorized by 21 USC 357(f) and 371(f) . . ." (Pet. Br. 9), and emphasizes that the Commissioner's determination was made "in a rule-making proceeding" (Pet. Br. 14).

Respondent has challenged no regulation in this proceeding, for there is, in fact, none applicable to the Bacto-Unidisk. Bacto-Unidisks contain sulfadiazine, which is not an antibiotic substance. Both the administrative determination that sensitivity disks are certifiable antibiotics and the regulations [46] pertaining to certification of disks apply only to disks containing antibiotics. Respondent, therefore, is attacking the legal conclusion that sen-

[46] See 21 CFR 146.10 and 147.2(b).

sitivity disks containing antibiotic substances are drugs, and is not attacking a regulation.

In any event, even if the Commissioner's administrative determination were applicable to Bacto-Unidisks, it could be attacked in this enforcement proceeding. It is true as stated by petitioner (Pet. Br. 9) that under 507 (f) and 701(f) judicial review may be obtained of an order issued pursuant to section 507(f). Although the Notice of Proposed Rule Making which originated the proceedings resulting in the order in question purported to be issued under Subsection (f) of section 507, the Notice was not authorized by that subsection since the Notice specifically stated it was made by the Commissioner "on his own initiative" (25 F.R. 3084). The Notice could therefore have been issued only under 507(a), which does not incorporate the provisions for judicial review contained in 701(f), as does section 507(f). Consequently, even persons marketing disks to which the regulations apply had no right to seek review in a Court of Appeals.[47]

Moreover, collateral attack upon administrative determinations is barred only if the statutory remedy of judicial review is exclusive. Thus, even if the procedures under section 701 were available to respondent, section 701 (f) (6) provides that the remedies under 701 "shall be in addition to and not in substitution for any other remedies provided by law." In a recent decision, this Court rejected the Government's attempt to narrowly construe section 701 (f) (6), stating that the clause should be taken "at its face value" and read "in harmony with the policy favoring judicial review expressed in the Administrative

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[47] Statutory authorization is, of course, required for direct appeals from administrative decisions to Courts of Appeals.

Procedure Act and this Court's decisions" *Abbott Laboratories* v. *Gardner*, 387 U.S. 136, 146.

The fact that the Secretary's (Commissioner's) interpretation of the statute extending its coverage to sensitivity disks, was made in a rule-making proceeding, endows it with no aura of sanctity. The interpretation was just like any other statutory interpretation by an administrative official. As stated by the Court of Appeals below, the function of the reviewing court in this case ". . . is not to review the validity of the regulations to determine if they are supportable by substantial record evidence and not an abuse of administrative discretion, but to determine, based upon an interpretation of the statutory definition of a drug, whether the seized article is within the administrator's jurisdiction" (App. 202).

CONCLUSION

For the reasons stated, it is respectfully submitted that the decisions below were clearly correct and that the judgment of the court of appeals should be affirmed.

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